

SEQUENCE LISTING

<110> CHANG, Y-H
 VETRO, J.A.
 MICKA, W.S.

<120> Dominant Negative Variants of Methionine Aminopeptidase
 2 ("MetAP2") and Clinical Uses Therefor

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<140>
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<170> PatentIn Ver. 2.0

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 Asp Asp Glu Asp Gly Asp Gly Asp Gly Asp Gly Ala Thr Gly Lys Lys
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 Lys Lys Lys Lys Lys Lys Lys
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 Glu Ser Asp Pro Val Glu Ser Lys Lys Lys Lys Asn Lys Lys Lys Lys
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 Lys Lys Lys Ser Asn Val Lys Lys Ile
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 35 40 45
 Ser Ala Ala Gly Glu Gln Glu Pro Asp Lys Glu Ser Gly Ala Ser Val
 50 55 60
 Asp Glu Val Ala Arg Gln Leu Glu Arg Ser Ala Leu Glu Asp Lys Glu
 65 70 75 80
 Arg Asp Glu Asp Asp Glu Asp Gly Asp Gly Asp Gly Asp Gly Ala Thr
 85 90 95
 Gly Lys Lys Lys Lys Lys Lys Lys Lys Lys Arg Gly Pro Lys Val Gln
 100 105 110
 Thr Asp Pro Pro Ser Val Pro Ile Cys Asp Leu Tyr Pro Asn Gly Val
 115 120 125
 Phe Pro Lys Gly Gln Glu Cys Glu Tyr Pro Pro Thr Gln Asp Gly Arg
 130 135 140
 Thr Ala Ala Trp Arg Thr Thr Ser Glu Glu Lys Lys Ala Leu Asp Gln
 145 150 155 160
 Ala Ser Glu Glu Ile Trp Asn Asp Phe Arg Glu Ala Ala Glu Ala His
 165 170 175
 Arg Gln Val Arg Lys Tyr Val Met Ser Trp Ile Lys Pro Gly Met Thr
 180 185 190

Met Ile Glu Ile Cys Glu Lys Leu Glu Asp Cys Ser Arg Lys Leu Ile
195 200 205

Lys Glu Asn Gly Leu Asn Ala Gly Leu Ala Xaa Pro Thr Gly Cys Ser
210 215 220

Leu Asn Asn Cys Ala Ala Xaa Tyr Thr Pro Asn Ala Gly Asp Thr Thr
225 230 235 240

Val Leu Gln Tyr Asp Asp Ile Cys Lys Ile Xaa Phe Gly Thr His Ile
245 250 255

Ser Gly Arg Ile Ile Xaa Cys Ala Phe Thr Val Thr Phe Asn Pro Lys
260 265 270

Tyr Asp Thr Leu Leu Lys Ala Val Lys Asp Ala Thr Asn Thr Gly Ile
275 280 285

Lys Cys Ala Gly Ile Asp Val Arg Leu Cys Asp Val Gly Glu Ala Ile
290 295 300

Gln Glu Val Met Glu Ser Tyr Glu Val Glu Ile Asp Gly Lys Thr Tyr
305 310 315 320

Gln Val Lys Pro Ile Arg Asn Xaa Asn Gly Xaa Ser Ile Gly Gln Tyr
325 330 335

Arg Xaa Xaa Ala Gly Lys Thr Val Pro Ile Val Lys Gly Gly Glu Ala
340 345 350

Thr Arg Met Glu Glu Gly Glu Val Tyr Ala Ile Xaa Thr Phe Gly Ser
355 360 365

Thr Gly Lys Gly Val Val His Asp Asp Met Glu Cys Ser His Tyr Met
370 375 380

Lys Asn Phe Asp Val Gly His Val Pro Ile Arg Leu Pro Arg Thr Lys
385 390 395 400

His Leu Leu Asn Val Ile Asn Glu Asn Phe Gly Thr Leu Ala Phe Cys
405 410 415

Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu
420 425 430

Lys Asn Leu Cys Asp Leu Gly Ile Val Asp Pro Xaa Pro Pro Xaa Cys
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 35 40 45
 Val Ser Ala Val Gln Gln Glu Leu Asp Lys Glu Ser Gly Ala Leu Val
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Asp Glu Ser Asp Pro Val Glu Ser Lys Lys Lys Lys Asn Lys Lys Lys
      35          40          45

Lys Lys Lys Lys Ser Asn Val Lys Lys Ile Glu Leu Leu Phe Pro Asp
      50          55          60

Gly Lys Tyr Pro Glu Gly Ala Trp Met Asp Tyr His Gln Asp Phe Asn
      65          70          75          80

Leu Gln Arg Thr Thr Asp Glu Glu Ser Arg Tyr Leu Lys Arg Asp Leu
      85          90          95

Glu Arg Ala Glu His Trp Asn Asp Val Arg Lys Gly Ala Glu Ile His
      100          105          110

Arg Arg Val Arg Arg Ala Ile Lys Asp Arg Ile Val Pro Gly Met Lys
      115          120          125

Leu Met Asp Ile Ala Asp Met Ile Glu Asn Thr Thr Arg Lys Tyr Thr
      130          135          140

Gly Ala Glu Asn Leu Leu Ala Met Glu Asp Pro Lys Ser Gln Gly Ile
      145          150          155          160

Gly Xaa Pro Thr Gly Leu Ser Leu Asn His Cys Ala Ala Xaa Phe Thr
      165          170          175

Pro Asn Ala Gly Asp Lys Thr Val Leu Lys Tyr Glu Asp Val Met Lys
      180          185          190

Val Xaa Tyr Gly Val Gln Val Asn Gly Asn Ile Ile Xaa Ser Ala Phe
      195          200          205

Thr Val Ser Phe Asp Pro Gln Tyr Asp Asn Leu Leu Ala Ala Val Lys
      210          215          220

Asp Ala Thr Tyr Thr Gly Ile Lys Glu Ala Gly Ile Asp Val Arg Leu
      225          230          235          240

Thr Asp Ile Gly Glu Ala Ile Gln Glu Val Met Glu Ser Tyr Glu Val
      245          250          255

Glu Ile Asn Gly Glu Thr Tyr Gln Val Lys Pro Cys Arg Asn Xaa Cys
      260          265          270

Gly Xaa Ser Ile Ala Pro Tyr Arg Xaa Xaa Gly Gly Lys Ser Val Pro
      275          280          285

Ile Val Lys Asn Gly Asp Thr Thr Lys Met Glu Glu Gly Glu His Phe
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<210> 12

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<213> Human MetAP2

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          35          40          45

Ser Ala Ala Gly Glu Gln Glu Pro Asp Lys Glu Ser Gly Ala Ser Val
          50          55          60

Asp Glu Val Ala Arg Gln Leu Glu Arg Ser Ala Leu Glu Asp Lys Glu
          65          70          75          80

Arg Asp Glu Asp Asp Glu Asp Gly Asp Gly Asp Gly Asp Gly Ala Thr
          85          90          95

Gly Lys Lys Lys Lys Lys Lys Lys Lys Arg Gly Pro Lys Val Gln
          100          105          110

Thr Asp Pro Pro Ser Val Pro Ile Cys Asp Leu Tyr Pro Asn Gly Val
          115          120          125

Phe Pro Lys Gly Gln Glu Cys Glu Tyr Pro Pro Thr Gln Asp Gly Arg
          130          135          140

Thr Ala Ala Trp Arg Thr Thr Ser Glu Glu Lys Lys Ala Leu Asp Gln
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Ala Ser Glu Glu Ile Trp Asn Asp Phe Arg Glu Ala Ala Glu Ala His
          165          170          175

Arg Gln Val Arg Lys Tyr Val Met Ser Trp Ile Lys Pro Gly Met Thr
          180          185          190

Met Ile Glu Ile Cys Glu Lys Leu Glu Asp Cys Ser Arg Lys Leu Ile
          195          200          205

Lys Glu Asn Gly Leu Asn Ala Gly Leu Ala Phe Pro Thr Gly Cys Ser
          210          215          220

Leu Asn Asn Cys Ala Ala His Tyr Thr Pro Asn Ala Gly Asp Thr Thr
          225          230          235          240

Val Leu Gln Tyr Asp Asp Ile Cys Lys Ile Asp Phe Gly Thr His Ile
          245          250          255

Ser Gly Arg Ile Ile Asp Cys Ala Phe Thr Val Thr Phe Asn Pro Lys
          260          265          270

Tyr Asp Thr Leu Leu Lys Ala Val Lys Asp Ala Thr Asn Thr Gly Ile
          275          280          285

Lys Cys Ala Gly Ile Asp Val Arg Leu Cys Asp Val Gly Glu Ala Ile
          290          295          300

Gln Glu Val Met Glu Ser Tyr Glu Val Glu Ile Asp Gly Lys Thr Tyr
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Gln Val Lys Pro Ile Arg Asn Leu Asn Gly His Ser Ile Gly Gln Tyr
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 370 375 380
 Lys Asn Phe Asp Val Gly His Val Pro Ile Arg Leu Pro Arg Thr Lys
 385 390 395 400
 His Leu Leu Asn Val Ile Asn Glu Asn Phe Gly Thr Leu Ala Phe Cys
 405 410 415
 Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu
 420 425 430
 Lys Asn Leu Cys Asp Leu Gly Ile Val Asp Pro Tyr Pro Pro Leu Cys
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 50 55 60
 Asp Glu Val Ala Lys Gln Leu Glu Ser Gln Ala Leu Glu Glu Lys Glu
 65 70 75 80
 Arg Asp Asp Asp Asp Glu Asp Gly Asp Gly Asp Ala Asp Gly Ala Thr
 85 90 95
 Gly Lys Lys Lys Lys Lys Lys Lys Lys Arg Gly Pro Lys Val Gln
 100 105 110
 Thr Asp Pro Pro Ser Val Pro Ile Cys Asp Leu Tyr Pro Asn Gly Val
 115 120 125
 Phe Pro Lys Gly Gln Glu Cys Glu Tyr Pro Pro Thr Gln Asp Gly Arg
 130 135 140
 Thr Ala Ala Trp Arg Thr Thr Ser Glu Glu Lys Lys Ala Leu Asp Gln
 145 150 155 160
 Ala Ser Glu Glu Ile Trp Asn Asp Phe Arg Glu Ala Ala Glu Ala His
 165 170 175

Arg Gln Val Arg Lys Tyr Val Met Ser Trp Ile Lys Pro Gly Met Thr
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 Met Ile Glu Ile Cys Glu Lys Leu Glu Asp Cys Ser Arg Lys Leu Ile
 195 200 205
 Lys Glu Asn Gly Leu Asn Ala Gly Leu Ala Phe Pro Thr Gly Cys Ser
 210 215 220
 Leu Asn Asn Cys Ala Ala His Tyr Thr Pro Asn Ala Gly Asp Thr Thr
 225 230 235 240
 Val Leu Gln Tyr Asp Asp Ile Cys Lys Ile Asp Phe Gly Thr His Ile
 245 250 255
 Ser Gly Arg Ile Ile Asp Cys Ala Phe Thr Val Thr Phe Asn Pro Lys
 260 265 270
 Tyr Asp Ile Leu Leu Thr Ala Val Lys Asp Ala Thr Asn Thr Gly Ile
 275 280 285
 Lys Cys Ala Gly Ile Asp Val Arg Leu Cys Asp Val Gly Glu Ala Ile
 290 295 300
 Gln Glu Val Met Glu Ser Tyr Glu Val Glu Ile Asp Gly Lys Thr Tyr
 305 310 315 320
 Gln Val Lys Pro Ile Arg Asn Leu Asn Gly His Ser Ile Gly Pro Tyr
 325 330 335
 Arg Ile His Ala Gly Lys Thr Val Pro Ile Val Lys Gly Gly Glu Ala
 340 345 350
 Thr Arg Met Glu Glu Gly Glu Val Tyr Ala Ile Glu Thr Phe Gly Ser
 355 360 365
 Thr Gly Lys Gly Val Val His Asp Asp Met Glu Cys Ser His Tyr Met
 370 375 380
 Lys Asn Phe Asp Val Gly His Val Pro Ile Arg Leu Pro Arg Thr Lys
 385 390 395 400
 His Leu Leu Asn Val Ile Asn Glu Asn Phe Gly Thr Leu Ala Phe Cys
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 Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu
 420 425 430
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<212> PRT

<213> Yeast MetAP2

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 50 55 60
 Gly Lys Tyr Pro Glu Gly Ala Trp Met Asp Tyr His Gln Asp Phe Asn
 65 70 75 80
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 Glu Arg Ala Glu His Trp Asn Asp Val Arg Lys Gly Ala Glu Ile His
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 Arg Arg Val Arg Arg Ala Ile Lys Asp Arg Ile Val Pro Gly Met Lys
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 Gly His Ser Ile Ala Pro Tyr Arg Ile His Gly Gly Lys Ser Val Pro
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 Ala Ile Glu Thr Phe Gly Ser Thr Gly Arg Gly Tyr Val Thr Ala Gly
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 Pro Thr Leu Asp Ser Ala Lys Asn Leu Leu Lys Thr Ile Asp Arg Asn
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Phe Gly Thr Leu Pro Phe Cys Arg Arg Tyr Leu Asp Arg Leu Gly Gln
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Glu Lys Tyr Leu Phe Ala Leu Asn Asn Leu Val Arg His Gly Leu Val
 370 375 380

Gln Asp Tyr Pro Pro Leu Asn Asp Ile Pro Gly Ser Tyr Thr Ala Gln
 385 390 395 400

Phe Glu His Thr Ile Leu Leu His Ala His Lys Lys Glu Val Val Ser
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 35 40 45

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Lys Lys Lys Lys Lys Lys Lys
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 35 40 45
 Val Ser Ala Gly Gln Gln Glu Leu Asp Lys Glu Ser Gly Thr Ser Val
 50 55 60
 Asp Glu Val Ala Lys Gln Leu Glu Arg Gln Ala Leu Glu Glu Lys Glu
 65 70 75 80
 Lys Asp Asp Asp Asp Glu Asp Gly Asp Gly Asp Gly Asp Gly Ala Ala
 85 90 95
 Gly Lys Lys Lys Lys Lys Lys Lys Lys Arg Gly Pro Arg Val Gln
 100 105 110
 Thr Asp Pro Pro Ser Val Pro Ile Cys Asp Leu Tyr Pro Asn Gly Val
 115 120 125
 Phe Pro Lys Gly Gln Glu Cys Glu Tyr Pro Pro Thr Gln Asp Gly Arg
 130 135 140
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 145 150 155 160

Ala Ser Glu Glu Ile Trp Asn Asp Phe Arg Glu Ala Ala Glu Ala His
 165 170 175
 Arg Gln Val Arg Lys Tyr Val Met Ser Trp Ile Lys Pro Gly Met Thr
 180 185 190
 Met Ile Glu Ile Cys Glu Lys Leu Glu Asp Cys Ser Arg Lys Leu Ile
 195 200 205
 Lys Glu Asn Gly Leu Asn Ala Gly Leu Ala Xaa Pro Thr Gly Cys Ser
 210 215 220
 Leu Asn Asn Cys Ala Ala Xaa Tyr Thr Pro Asn Ala Gly Asp Thr Thr
 225 230 235 240
 Val Leu Gln Tyr Asp Asp Ile Cys Lys Ile Xaa Phe Gly Thr His Ile
 245 250 255
 Ser Gly Arg Ile Ile Xaa Cys Ala Phe Thr Val Thr Phe Asn Pro Lys
 260 265 270
 Tyr Asp Ile Leu Leu Lys Ala Val Lys Asp Ala Thr Asn Thr Gly Ile
 275 280 285
 Lys Cys Ala Gly Ile Asp Val Arg Leu Cys Asp Val Gly Glu Ala Ile
 290 295 300
 Gln Glu Val Met Glu Ser Tyr Glu Val Glu Ile Asp Gly Lys Thr Tyr
 305 310 315 320
 Gln Val Lys Pro Ile Arg Asn Xaa Asn Gly Xaa Ser Ile Gly Pro Tyr
 325 330 335
 Arg Xaa Xaa Ala Gly Lys Thr Val Pro Ile Val Lys Gly Gly Glu Ala
 340 345 350
 Thr Arg Met Glu Glu Gly Glu Val Tyr Ala Ile Xaa Thr Phe Gly Ser
 355 360 365
 Thr Gly Lys Gly Val Val His Asp Asp Met Glu Cys Ser His Tyr Met
 370 375 380
 Lys Asn Phe Asp Val Gly His Val Pro Ile Arg Leu Pro Arg Thr Lys
 385 390 395 400
 His Leu Leu Asn Val Ile Asn Glu Asn Phe Gly Thr Leu Ala Phe Cys
 405 410 415
 Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu
 420 425 430
 Lys Asn Leu Cys Asp Leu Gly Ile Val Asp Pro Xaa Pro Pro Xaa Cys
 435 440 445
 Asp Ile Lys Gly Ser Tyr Thr Ala Gln Phe Xaa His Thr Ile Leu Cys
 450 455 460
 Ala Gln Pro Val Lys Lys Leu Ser Ala Glu Glu Met Thr Ile Lys Thr
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<210> 17
 <211> 480

<212> PRT

<213> Rat MetAP2

<400> 17

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Met Ala Gly Val Glu Glu Ala Ser Ser Phe Gly Gly His Leu Asn Arg
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Asp Leu Asp Pro Asp Asp Arg Glu Glu Gly Thr Ser Ser Thr Ala Glu
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Glu Ala Ala Lys Lys Lys Arg Arg Lys Lys Lys Gly Lys Gly Ala
      35           40           45

Val Ser Ala Gly Gln Gln Glu Leu Asp Lys Glu Ser Gly Thr Ser Val
      50           55           60

Asp Glu Val Ala Lys Gln Leu Glu Arg Gln Ala Leu Glu Glu Lys Glu
      65           70           75           80

Lys Asp Asp Asp Asp Glu Asp Gly Asp Gly Asp Gly Asp Gly Ala Ala
      85           90           95

Gly Lys Lys Lys Lys Lys Lys Lys Lys Arg Gly Pro Arg Val Gln
      100          105          110

Thr Asp Pro Pro Ser Val Pro Ile Cys Asp Leu Tyr Pro Asn Gly Val
      115          120          125

Phe Pro Lys Gly Gln Glu Cys Glu Tyr Pro Pro Thr Gln Asp Gly Arg
      130          135          140

Thr Ala Ala Trp Arg Thr Thr Ser Glu Glu Lys Lys Ala Leu Asp Gln
      145          150          155          160

Ala Ser Glu Glu Ile Trp Asn Asp Phe Arg Glu Ala Ala Glu Ala His
      165          170          175

Arg Gln Val Arg Lys Tyr Val Met Ser Trp Ile Lys Pro Gly Met Thr
      180          185          190

Met Ile Glu Ile Cys Glu Lys Leu Glu Asp Cys Ser Arg Lys Leu Ile
      195          200          205

Lys Glu Asn Gly Leu Asn Ala Gly Leu Ala Phe Pro Thr Gly Cys Ser
      210          215          220

Leu Asn Asn Cys Ala Ala His Tyr Thr Pro Asn Ala Gly Asp Thr Thr
      225          230          235          240

Val Leu Gln Tyr Asp Asp Ile Cys Lys Ile Asp Phe Gly Thr His Ile
      245          250          255

Ser Gly Arg Ile Ile Asp Cys Ala Phe Thr Val Thr Phe Asn Pro Lys
      260          265          270

Tyr Asp Ile Leu Leu Lys Ala Val Lys Asp Ala Thr Asn Thr Gly Ile
      275          280          285

Lys Cys Ala Gly Ile Asp Val Arg Leu Cys Asp Val Gly Glu Ala Ile
      290          295          300

Gln Glu Val Met Glu Ser Tyr Glu Val Glu Ile Asp Gly Lys Thr Tyr
      305          310          315          320

Gln Val Lys Pro Ile Arg Asn Leu Asn Gly His Ser Ile Gly Pro Tyr
      325          330          335

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Arg Ile His Ala Gly Lys Thr Val Pro Ile Val Lys Gly Gly Glu Ala
      340                      345                      350

Thr Arg Met Glu Glu Gly Glu Val Tyr Ala Ile Glu Thr Phe Gly Ser
      355                      360                      365

Thr Gly Lys Gly Val Val His Asp Asp Met Glu Cys Ser His Tyr Met
      370                      375                      380

Lys Asn Phe Asp Val Gly His Val Pro Ile Arg Leu Pro Arg Thr Lys
      385                      390                      395                      400

His Leu Leu Asn Val Ile Asn Glu Asn Phe Gly Thr Leu Ala Phe Cys
      405                      410                      415

Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu
      420                      425                      430

Lys Asn Leu Cys Asp Leu Gly Ile Val Asp Pro Tyr Pro Pro Leu Cys
      435                      440                      445

Asp Ile Lys Gly Ser Tyr Thr Ala Gln Phe Glu His Thr Ile Leu Cys
      450                      455                      460

Ala Gln Pro Val Lys Lys Leu Ser Ala Glu Glu Met Thr Ile Lys Thr
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<210> 18
<211> 1944
<212> DNA
<213> Rat MetAP2 variant

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<220>
<221> misc_feature
<222> (779)
<223> Any nucleotide

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gacaagagtg tgaataccca cccacccaag atgggcggac agctgcttgg agaaccacaa 540
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caattgggcc atatagaatt catgctggaa aaacagtgcc cattgtgaaa ggagggaag 1140
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cagcagagga gatgactatt aaaacttagt ccaaagccaa ctcaacgtct ttattttcta 1560
agctttgttg gaacacatta taccacaagt aatttgcaac atgtctgttt taacagtgga 1620
cctgtgtaat gccgttatcc atgtttaaag gagtttgatc aaagccaaac tgtctacatg 1680
taattaacca aggaaaaggc tttcaagact ttactgttaa ctgtttctcc cgtctaggaa 1740
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tgctttttgg atatttatat tgccatattc ttacttggtg gctttgaatg actacataca 1860
tccagttctg cacctatgcc ctctggtatt gctttttaac cttcctggaa tccattttct 1920
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<210> 19

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: synthetic
transit peptide

<400> 19

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Gly Arg Lys Lys Arg Arg Gln Arg
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<210> 20

<211> 40

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: synthetic
oligonucleotide

<400> 20

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<210> 21

<211> 35

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: synthetic
oligonucleotide

<400> 21

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<210> 22

<211> 11

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: synthetic
peptide

<400> 22

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Cys Lys Glu Val Val Ser Lys Gly Asp Asp Tyr
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<210> 23

<211> 9

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: synthetic peptide

<400> 23

Tyr Pro Tyr Asp Val Pro Asp Tyr Ala
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<210> 24

<211> 4

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: synthetic peptide

<400> 24

Met Gly Met Met
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<210> 25

<211> 63

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: synthetic oligonucleotide

<400> 25

cacactcgac cgcgatgtac tactactact actactacta ctactacggg ccagatatac 60
gcg 63

<210> 26

<211> 37

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: synthetic oligonucleotide

<400> 26

cacagaattc cccgcatccc cagcatgcct gctattg

37